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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,982	04/02/2007	Robin Kurfurst	15675P620	2408

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,982	KURFURST ET AL.	
	Examiner	Art Unit	
	TERRA C. GIBBS	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38,42-57 and 60-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38, 42-57, and 60-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's Amendment and Remarks filed December 14, 2010.

Claims 38 and 57 have been amended. Claim 67 has been canceled.

Claims 38, 42-57, and 60-66 are pending in the instant application.

Claims 38, 42-57, and 60-66 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

In the previous Office Action mailed June 16, 2010, claims 38, 42-57, and 60-67 were rejected under 35 U.S.C. 103(a) as being unpatentable over WO 95/02069 A1, also referred to as "Bennett" (submitted and made of record on Applicant's Information Disclosure Statement filed November 20, 2006) in view of Park et al. (Journal of Biological Chemistry, 1993 Vol. 268:16:11742-11749, submitted and made of record on Applicant's Information Disclosure Statement filed November 20, 2006). **This rejection is moot** against claim 67 in view of Applicant's Amendment filed December 14, 2010 to cancel this claim. **This rejection is maintained** against claims 38, 42-57, and 60-66 for the reasons of record set forth in the previous Office Action mailed June 16, 2010.

Response to Arguments

In response to this rejection, Applicants argue that in regard to independent claims 38 and 57, Bennett in view of Park fails to disclose or render predictable at least the elements of "a topical pharmaceutical composition comprising at least one oligonucleotide having between 7 and 25 nucleotides, capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 (PKC beta-1) and modifying expression of only PKC beta-1" as recited in amended claims 38 and 57.

This argument has been considered, but is not found persuasive because contrary to Applicant's assertions, Bennett indeed discloses and renders predictable a topical pharmaceutical composition comprising at least one oligonucleotide having between 7 and 25 nucleotides, capable of specifically hybridizing with genes or gene products coding for protein kinase C beta-1 (PKC beta-1) and modifying expression of only PKC beta-1. See Table 3, for example. Also, see claims 70, 72, 85, 89, and 90 and specifically SEQ ID NOs. 25-29, for example.

Applicants next argue that while Bennett may suggest oligonucleotides targeting PKC beta-1 only, and thus suggests the use of a PKC beta-1 specific oligonucleotide if needed, it is important to highlight that Bennett may only provide motivation to use such oligonucleotides for the treatment of diseases associated to PKC beta-1 only. Applicants contend that the main teaching of Bennett is thus that, for the treatment of a particular disease, one of ordinary skill in the art should use oligonucleotides specific for one or more PKC isoforms that are known to be associated to this particular disease. That is, the teachings of Bennett are that specific oligonucleotides should be used

depending on the knowledge concerning which PKC isoform(s) is/are associated to a particular disease.

This argument has been fully considered, but is not found persuasive because Bennett teach oligonucleotides targeted to both PKC beta 1 and PKC beta-2 (Table 2); oligonucleotides targeted to PKC beta 1 only (Table 3); and oligonucleotides targeted to PKC beta 2 only (Table 4). However, Bennett also disclose and claim a method of treating a condition associated with expression of PKC comprising administering to a mammal a therapeutically effective amount of an oligonucleotide having 5 to 50 nucleotides units specifically hybridizable with a PKC gene or mRNA. See claim 70. Bennett also discloses and claims that the condition associated with the expression of PKC is a hyperproliferative disorder being psoriasis. See claims 71 and 72. Bennett also discloses and claims that the PKC gene is specifically PKC beta-1 (see claims 85, 89, and 90 and SEQ ID NOs: 25-29).

Furthermore, and as noted in the previous Office Action mailed June 16, 2010 at pages 7 and 8, it is noted that Bennett do not explicitly teach that the topical administration of antisense oligonucleotides targeted PKC beta-1 will result in a method of depigmenting or bleaching human skin. However, Applicant is reminded that the burden of establishing whether the teachings of Bennett would have the additional function of resulting in a depigmenting effect, under generally any assay conditions falls to Applicant. See MPEP 2112.02.

Applicants next argue that neither Bennett nor Park alone disclose a method of depigmenting or bleaching human skin, body hair or hair on a head of a subject using a

topical composition capable of modifying expression of only PKC beta 1 as claimed in the instant Application.

This argument has been fully considered, but is not found persuasive because as discussed *supra*, Bennett disclose a method of depigmenting or bleaching human skin using a topical composition capable of modifying expression of only PKC beta 1 as claimed in the instant Application, absent evidence to the contrary. For example, Bennett disclose and claim a method of treating a condition associated with expression of PKC comprising administering to a mammal a therapeutically effective amount of an oligonucleotide having 5 to 50 nucleotides units specifically hybridizable with a PKC gene or mRNA. See claim 70. Bennett also discloses and claims that the condition is a hyperproliferative disorder being psoriasis. See claims 71 and 72. Bennett also discloses and claims that the PKC gene is specifically PKC beta-1 (see claims 85, 89, and 90 and SEQ ID NOs: 25-29).

As noted in the previous Office Action mailed June 16, 2010 at pages 7 and 8, it is noted that Bennett do not explicitly teach that the topical administration of antisense oligonucleotides targeted PKC beta-1 will result in a method of depigmenting or bleaching human skin. However, Applicant is reminded that the burden of establishing whether the teachings of Bennett would have the additional function of resulting in a depigmenting effect, under generally any assay conditions falls to Applicant. See MPEP 2112.02.

Furthermore, by using the method steps disclosed by Bennett, it is the Examiner's position that a method of depigmenting or bleaching human skin as instantly

claimed would be inherent to Bennett, absent evidence to the contrary. See MPEP 2112.02. This is primarily due to the fact that the method steps of Bennett are the exact method steps of Applicant's claimed invention, being the administration of an oligonucleotide specifically hybridizable to PKC beta and modifying expression of only PKC beta-1. Therefore, the methods of Bennett will carry out the functionality of Applicant's claimed invention, absent some evidence to the contrary.

Applicants next argue that Park only refers to PKC beta, without indicating which isoform of PKC beta has been tested. Applicants contend that this teachings would have been interpreted by one of ordinary skill in the art, at the time of invention, as involving both PKC beta-1 and PKC-beta-2 in melanogenesis. Applicants also point the Examiner to the 37 CRF §1.132 Declaration provided on December 14, 2010 and the teachings of Nishizuka. Applicants argue that in view of the teachings of Nishizuka, one of ordinary skill in the art would have concluded that PKC beta-1 and beta-2 isoforms most probably have about the same functions, and would thus having been incited, based on Park, to inhibit both isoforms for depigmentation applications.

This argument has been fully considered, but is not persuasive. Furthermore, Applicant's 37 CRF §1.132 Declaration provided on December 14, 2010 has been considered, but has not been persuasive. The main reason why these have not been found persuasive is because Bennett teaches a method of treating a condition associated with PKC beta expression comprising topically administering an oligonucleotide that specifically hybridizes with PKC beta. See claim 70 and page 18, lines 6-9. Bennett goes on to teach that the oligonucleotide that specifically hybridizes

with PKC beta is specific for PKC beta-1 only. See Table 3 at SEQ ID NOs: 25-29.

By using the method steps disclosed by Bennett, a method of depigmenting or bleaching human skin as instantly claimed would be inherent to Bennett, absent evidence to the contrary. See MPEP 2112.02. Thus, the Examiner maintains Her position that the method steps of Bennett are the exact method steps of Applicant's invention, namely the administration of an oligonucleotide specifically hybridizable to PKC beta and modifying expression of only PKC beta-1. Therefore, the methods of Bennett will carry out the functionality of Applicant's claimed invention, absent some evidence to the contrary.

Applicants next argue that despite the fact that the prior art globally deterred one of ordinary skill in the art to target PKC beta-1 only for depigmentation purposes, the inventors of the instant Application found *unexpectedly* that the specific targeting of PKC beta-1 is sufficient to inhibit melanogenesis. Applicants point the Examiner to the 37 CRF §1.132 Declaration provided on December 14, 2010 and Examples 2 to 4 of the instant application.

This argument has been fully considered, but is not found persuasive because while the prior art of Park taught that both PKC beta-1 and PKC-beta-2 are involved in melanogenesis, the prior art of Bennett clearly motivated one in the art to inhibit both PKC beta-1 and PKC beta-2 (Table 2); PKC beta-1 alone (Table 3); or PKC beta-2 alone (Table 4). Thus, Bennett provided the motivation to inhibit one PKC isoform over another. Therefore, one of skill in the art would have applied the teachings and motivation provided by Bennett to arrive at Applicant's claimed invention, absent some

evidence to the contrary. Thus, the specific targeting of PCK beta-1 is not unexpected since Bennett provided clear and explicit motivation for one of ordinary skill in the art to do so.

Furthermore, the specific targeting of PKC beta-1 to inhibit melanogenesis is not unexpected because the single method step involved for such inhibition is taught by Bennett and therefore the methods of Bennett will carry out such functionality, absent evidence to the contrary.

In view of the foregoing, when all the evidence is considered, the totality of the rebuttal evidence of non-obviousness fails to outweigh the evidence of obviousness made of record. Thus, it is maintained that the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was filed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached from 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Heather Calamita can be reached on 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Terra Cotta Gibbs/
March 8, 2011

/Sean R McGarry/

Primary Examiner, Art Unit 1635